DETAILED ACTION

This office action is a response to Applicant's amendment submitted July 1, 2009, wherein claim 7 is amended and claim 13 is newly submitted.

Claims 7-13 are pending and are examined on the merits herein.

In view of Applicant's amendment submitted July 1, 2009, the rejection of claims 7-12 under 35 U.S.C. 112, first paragraph, for lacking enablement for prevention of recurrent oral aphthous ulcers is withdrawn.

The following rejection of record is maintained:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Di Schiena (EP 0444492, April 9, 1991, PTO-1449 submitted May 3, 2007) in view of Saxen et al. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997; 84:356-61, of record).

Di Schiena teaches pharmaceutical compositions comprising 0.2 to 10% sodium hyaluronate having molecular weight between 800,000-4,000,000, preferably

1,000,000-2,000,000 [page 2, line 52] for the treatment and prophylaxis of inflammatory affections of the oral cavity [claims 1-10].

Di Schiena does not exemplify the treatment of recurrent oral aphthous ulcers using the composition.

Saxen teaches that recurrent aphthous ulcers are a common disorder, causing pain derived from inflammatory sensitization of nerve endings, and the most common treatment is topical anesthetics and topical steroids for pain management [page 356, first two paragraphs]. Adults having aphthous ulcers were treated with 3% diclofenac in 2.5% hyaluronan, 2.5% hyaluronan, or 3% viscous lidocaine. A 48% reduction in pain was observed 10 minutes after application with no significant difference between the three topical agents [see abstract]. Ulcers were smaller after treatment with HA [page 359, Table 1]. The blunting action of hyaluronan may be due to the coating action over the ulcer [page 360, second full paragraph], and the protective layering of the ulcer was a significant component of the overall treatment effect [page 360, third full paragraph].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use Di Schiena's composition for the treatment of recurrent aphthous ulcers. Di Schiena teaches that HA of molecular weight 1,000,000-2,000,000 is useful for treating inflammatory affections of the oral cavity, including stomatitis, but does not specifically mention recurrent aphthous ulcers. Saxen teaches that HA alone can be used to treat recurrent aphthous ulcers, resulting in a reduction in pain and smaller ulcers, but is silent with respect to the molecular weight of the HA. The skilled artisan could expect that Di Schiena's composition would be useful for the treatment of

a specific inflammatory affection of the oral cavity, recurrent oral aphthous ulcers, because Saxen teaches that HA is effective for treatment of recurrent oral aphthous ulcers. The skilled artisan could expect that HA of molecular weight 1,000,000-2,000,000 could be effectively used in the method taught by Saxen because Di Schiena teaches that HA of that molecular weight is useful for treatment of inflammatory conditions of the mouth. Thus, the claimed invention is obvious over the prior art.

Response to Arguments

Applicant argues that Saxen teaches that diclofenac/HA is better than HA alone for treatment of recurrent oral aphthous ulcers, that HA only reduces pain immediately after treatment, and that the examiner is using hindsight reconstruction. This argument has been carefully considered but is not persuasive.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In this case, the rejection relies only upon knowledge which was within the level of ordinary skill at the time the claimed invention was made. Di Schiena teaches a hyaluronic acid composition which is useful for treatment of inflammatory affections of the oral cavity, including stomatitis. The skilled artisan would understand that stomatitis

is a broad condition which encompasses recurrent oral aphthous ulcers. Saxen teaches that topical application of HA provides immediate pain relief for recurrent aphthous ulcers, even in the absence of other active ingredients. Although HA was inferior to HA/diclofenac after 1 hour, immediate pain relief is clearly taught. Saxen also teaches that lesion size decreased slightly after treatment with HA alone [see Table 1]. Applicant argues that these results are not significant because the test lasted 8 hours, and pain relief with HA alone is most effective early in the test. This argument is not persuasive because Saxen clearly teaches treatment with HA alone, which results in immediate pain relief. MPEP 2123 states: "A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill in the art, including nonpreferred embodiments," and "Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments." Thus, although Saxen teaches that diclofenac-HA is more effective than HA alone, it is clear that HA alone does provide benefits such as immediate pain relief and small reduction in lesion size.

Applicant argues that Saxen teaches "no significant change in ulcer diameter." Table 1 does show a decrease in lesion size after treatment. Pretreatment lesion size was 5.0 (3-9) and posttreatment lesion size was 4.58 (0-6). Although Saxen states that the change is not significant, Table 1 clearly teaches that there was a reduction in lesion size. The maximum lesion size went from 9 to 6, a 30% reduction, and the smallest ulcer size went from 3 to 0.

Applicant argues that the reduction in pain is due to coating action of HA, not by therapeutic effect. This argument is not persuasive because the cited references teach treatment of ROAU using HA. Reduction in pain and lesion size is a therapeutic effect, and is treatment.

Applicant argues that Annex 1 filed September 26, 2008 shows that HA unexpectedly causes reduction of ulcers and new ulcer occurrence. The results Applicant refers to occurred on days 4-7 of administration with application 2-3 times daily. Saxen's subjects were only administered HA one time, with follow-up within 24 to 72 hours. Saxen's subjects had a small decrease in lesion size [see Table 1] after one application, so the skilled artisan could expect further reduction over 7 days. At least one of Saxen's subjects had a lesion size of 0 after one application, so the skilled artisan could expect a reduced number of lesions after 7 days. Furthermore, Di Schiena teaches that HA is effective for the prophylaxis of inflammatory conditions of the oral cavity [see claim 1], so the skilled artisan could expect a reduced number of new lesions after application. For these reasons, the data shown in Annex 1 is not unexpected. Furthermore, the claims are not of the same scope as the data in Annex 1. See MPEP 716.02(d): Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support." In other words, the showing the unexpected results must be reviewed to see if the results occur over the entire claimed range. The results in Annex

1 require multiple administrations of a minimum concentration of HA over a number of days, which is not required by the instant claims.

For these reasons, the rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on Monday - Friday, 7:00 - 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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